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PATENT

DOCKET NO.: ISIS-4785

TECH CENTER 1600/2900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Vasulinga T. Ravikumar

Serial No.: 09/881,535

Filed: June 14, 2001

For: METHODS FOR PREPARING OLIGONUCLEOTIDES HAVING CHIRAL  
PHOSPHOROTHIOATE LINKAGES

Confirmation No.: 8150

Group Art Unit: 1635

Examiner: Janet L. Epps

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

#### ASSOCIATE POWER OF ATTORNEY

The undersigned, of the firm WOODCOCK WASHBURN LLP, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, Attorney(s) and/or Agents for Applicant(s), hereby appoints the all the practitioners associated with Customer Number 32,650 his or her associates with full power to prosecute this application and to transact all business in the U.S. Patent and Trademark Office connected therewith. Each practitioner associated with Customer Number 32,650 is an attorney registered before the United States Patent and Trademark Office.



32650

Date: March 28, 2003

John W. Caldwell  
Registration No. 28,937

Woodcock Washburn LLP  
One Liberty Place - 46th Floor  
Philadelphia PA 19103  
Telephone: (215) 568-3100  
Facsimile: (215) 568-3439



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DEC 31 2001

Woodcock Washburn Kurtz  
Mackiewicz & Norris LLP



*Jwe/MPs/ScT*

DECEMBER 20, 2001

WOODCOCK WASHBURN LLP  
JOHN W. CALDWELL  
ONE LIBERTY PLACE - 46TH FLOOR  
PHILADELPHIA, PA 19103-7301

Under Secretary of Commerce For Intellectual Property and  
Director of the United States Patent and Trademark Office  
Washington, DC 20231  
www.uspto.gov

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\*101878985A\*

UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

*ISIS-4785*

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 10/11/2001

REEL/FRAME: 012251/0360  
NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

RAVIKUMAR, VASULINGA T.

DOC DATE: 10/08/2001

ASSIGNEE:

ISIS PHARMACEUTICALS, INC.  
2292 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008

SERIAL NUMBER: 09881535  
PATENT NUMBER:

FILING DATE: 06/14/2001  
ISSUE DATE:

RECEIVED

MARGARET LASALLE, PARALEGAL  
ASSIGNMENT DIVISION  
OFFICE OF PUBLIC RECORDS

APR 02 2003

TECH CENTER 1500 2000

COPIES TO CLIENT

1/10/02

10-19-2001



101878985

10-11-01

To The Honorable Commissioner of Patent

red original documents or copy thereof.

1. Name of conveying party(ies):

**VASULINGA T. RAVIKUMAR**

First Assignor

Date of Execution

Second Assignor

Date of Execution

Third Assignor

Date of Execution

Fourth Assignor

Date of Execution

Fifth Assignor

Date of Execution

Sixth Assignor

Date of Execution

Additional name(s) of conveying party(ies) attached? ( ) YES (X) NO

2. Name and address of receiving party(ies):

Name: **ISIS PHARMACEUTICALS, INC.**

Street Address: 2292 Faraday Avenue

City: Carlsbad

State

CA

ZIP 92008

Additional name(s) &amp; address attached? ( ) YES (X) NO

3. Nature of Conveyance (check only one):

☒ (X) New Assignment☐ ( ) Merger☐ ( ) License Agreement☐ ( ) Security Agreement☐ ( ) Change of Name☐ ( ) Other:☐ ( ) Cross-reference of Assignment filed in United States

Application No. \_\_/\_\_, recorded on \_\_\_\_ at

Reel No. \_\_\_\_ and Frame No. \_\_\_\_

4. Identification of Application number(s), patent number(s) OR date of execution of application to which assignment refers:

Application Nos.:

**09/881,535**

Patent Nos.:

Date application was signed by the first  
named executing inventor(Fill-in this date only if assignment is  
filed together with a new application)5. Name and address of party to whom correspondence  
concerning documents should be mailed:Name: **JOHN W. CALDWELL, ESQUIRE**  
**WOODCOCK WASHBURN LLP**  
One Liberty Place - 46th Floor  
Philadelphia, Pennsylvania 19103-7301  
215-568-31006. Total number of applications and patents involved: 1

7. Total fee (37 CFR 3.41):.....\$40.00

☒ (x) Enclosed☐ ( ) Authorized to be charged to Deposit Account  
Number 23-30508. Please charge any deficiency or credit any  
overpayment to Deposit Account Number 23-3050

DO NOT USE THIS SPACE

9. Statement and signature.

*To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.***JOHN W. CALDWELL/28,937**

Name of Person Signing/Reg. No.

Signature

October 9, 2001

Date

Total number of pages including cover sheet, assignment document and additional pages attached thereto: 3

Mail documents to be recorded with required cover sheet information to:

Commissioner of Patents and Trademarks  
Box Assignments  
Washington, D.C. 20231

ASSIGNMENT

WHEREAS, I, **Vasulinga T. Ravikumar**, of 6606 Vireo Court, Carlsbad, California, have invented a certain invention entitled **METHODS FOR PREPARING OLIGONUCLEOTIDES HAVING CHIRAL PHOSPHOROTHIOATE LINKAGES**, for which we have made application for Letters Patent of the United States, said application having been filed on **June 14, 2001** as Serial Number **09/881,535**; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its

successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible, to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

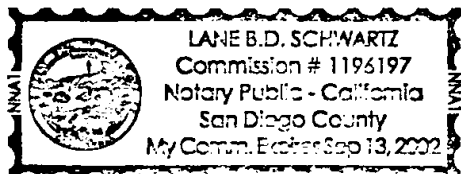
Dated: October 8<sup>th</sup> year of 2001

V. T. Ravikumar  
Vasulinga T. Ravikumar

State of California                    )  
  )     ss.  
County of San Diego                 )

On this 8<sup>th</sup> day of October, year of 2001, before me, the undersigned, a Notary Public for the state, personally appeared **Vasulinga T. Ravikumar** personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that ~~he/she~~ executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



[Signature]  
Signature of Notary



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

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FEBRUARY 24, 2000

PTAS

WOODCOCK WASHBURN KURTZ, ET AL.  
MICHAEL P. STRAHER  
ONE LIBERTY PLACE - 46TH FLOOR  
1650 MARKET STREET  
PHILADELPHIA, PENNSYLVANIA 19103-7301



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UNITED STATES PATENT AND TRADEMARK OFFICE  
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

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PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231..

RECORDATION DATE: 11/18/1999

REEL/FRAME: 010399/0289  
NUMBER OF PAGES: 5

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:  
COOK, PHILLIP DAN

DOC DATE: 08/05/1999

ASSIGNOR:  
MANOHARAN, MUTHIAH

DOC DATE: 08/05/1999

ASSIGNEE:  
ISIS PHARMACEUTICALS, INC.  
2292 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008

SERIAL NUMBER: 09352058  
PATENT NUMBER:

FILING DATE: 07/14/1999  
ISSUE DATE:

KIMBERLY WHITE, EXAMINER  
ASSIGNMENT DIVISION  
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TECH CENTER 1600/2900

*Original to client 3/25/00*

12-01-1999

U.S. DEPARTMENT OF COMMERCE  
Patent and Trademark OfficeTo The Honorable Commissioner of Patent  
thereof.

101211405

Attached original documents or copy

## 1. Name of conveying party(ies):

Phillip Dan Cook and Muthiah Manoharan

Additional name(s) of conveying party(ies)  
attached? ( ) YES (X) NO

## 3. Nature of Conveyance:

(X) Assignment ( ) Merger

( ) Security Agreement

( ) Change of Name

( ) Other:

Execution Date(s): August 5, 1999

## 2. Name and address of receiving party(ies):

Name: ISIS Pharmaceuticals, Inc.

Street Address: 2292 Faraday Avenue

City: Carlsbad

State California

ZIP 92008

Additional name(s) &amp; address attached? ( ) YES (X) NO

## 4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s)

09/352,058 filed 07/14/99

B. Patent No.(s)

Additional numbers attached? ( ) YES (X) NO

5. Name and address of party to whom correspondence  
concerning documents should be mailed:

Name: Michael P. Straher

Internal Address: WOODCOCK WASHBURN KURTZ

MACKIEWICZ &amp; NORRIS LLP

One Liberty Place - 46th Floor

Philadelphia, Pennsylvania 19103-7301

Street Address: WOODCOCK WASHBURN KURTZ

MACKIEWICZ &amp; NORRIS LLP

One Liberty Place - 46th Floor

1650 Market Street

Philadelphia, Pennsylvania 19103-7301

## 6. Total number of applications and patents involved:

One (1)

## 7. Total fee (37 CFR 3.41):.....\$40.00

(X) Enclosed

( ) Authorized to be charged to Deposit Account  
Number 23-30508. Please charge any deficiency or credit any  
overpayment to Deposit Account Number 23-3050

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## 9. Statement and signature.

*To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.*

Michael P. Straher/38,325

Name of Person Signing/Reg. No.

Signature

November 16, 1999

Date

Total number of pages including cover sheet, attachments, and document: 5

Mail documents to be recorded with required cover sheet information to:

11/30/1999 DNGUYEN 00000176 09352058

FC:581

40.00

Commissioner of Patents and Trademarks  
Box Assignments  
Washington, D.C. 20231

## A S S I G N M E N T

WHEREAS, We, **Phillip Dan Cook, of Fallbrook, State of California and Muthiah Manoharan, of Carlsbad, State of California**, have invented a certain invention entitled **OLIGONUCLEOTIDES HAVING SITE SPECIFIC CHIRAL PHOSPHOROTHIOATE INTERNUCLEOSIDE LINKAGES**, for which we have made application for Letters Patent of the United States, said application having been **filed July 14, 1999 and assigned Application No. 09/352,058**; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee; of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

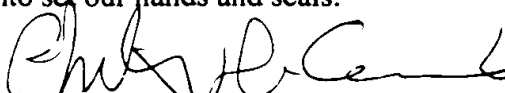
NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.



AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

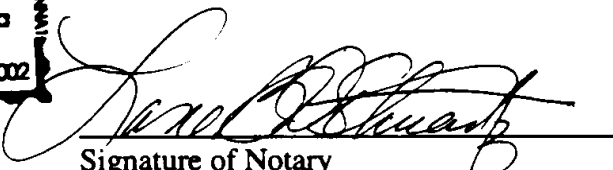
IN WITNESS WHEREOF, we have hereunto set our hands and seals.

Dated: 8/05/99, 1999  
PHILLIP DAN COOKState of California           )  
  )       ss.  
County of San Diego        )

On this 5<sup>th</sup> day of August, 1999, before me, the undersigned, a Notary Public for the state, personally appeared **PHILLIP DAN COOK** personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that ~~he~~she executed the same in ~~his~~her authorized capacity, and that by ~~his~~her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



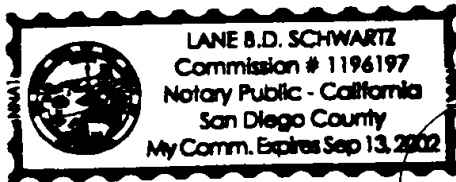
WITNESS my hand and official seal.

  
Signature of Notary

Dated: August 5, 1999Muthiah Manoharan  
MUTHIAH MANOHARAN

State of California            )  
  )       ss.  
County of San Diego         )

On this 5<sup>th</sup> day of August, 1999, before me, the undersigned, a Notary Public for the state, personally appeared **MUTHIAH MANOHARAN** personally known to me/~~proved to me on the basis of satisfactory evidence to be the~~ person who subscribed the foregoing Assignment and acknowledged to me that ~~he~~/she executed the same in ~~his~~/her authorized capacity, and that by ~~his~~/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Lane B.D. Schwartz  
Signature of Notary



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

JANUARY 12, 1999

PTAS

WOODCOCK WASHBURN KURTZ MACKIEWICZ &  
NORRIS LLP; MICHAEL P. STRAHER, ESQ.  
ONE LIBERTY PLACE - 46TH FLOOR  
1650 MARKET STREET  
PHILADELPHIA, PENNSYLVANIA 19103-7301



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JAN 19 1999

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**Woodcock Washburn Kurtz  
Mackiewicz & Norris LLP**

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PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, CG-4, 1213 JEFFERSON DAVIS HWY, SUITE 320, WASHINGTON, D.C. 20231.

RECORDATION DATE: 09/14/1998

REEL/FRAME: 9449/0621  
NUMBER OF PAGES: 5

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

ELEUTERI, ALESSANDRA

DOC DATE: 08/03/1998

ASSIGNOR:

CAPALDI, DANIEL C.

DOC DATE: 08/03/1998

ASSIGNOR:

RAVIKUMAR, VASULINGA T.

DOC DATE: 09/01/1998

ASSIGNEE:

ISIS PHARMACEUTICALS, INC.  
2292 FARADAY AVENUE  
CARLSBAD, CALIFORNIA 92008

SERIAL NUMBER: 09095811  
PATENT NUMBER:

FILING DATE: 06/11/1998  
ISSUE DATE:

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9449/0621 PAGE 2

ANTIONE ROYALE, EXAMINER  
ASSIGNMENT DIVISION  
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09-17-1998

3 SHEET

U.S. DEPARTMENT OF COMMERCE  
Patent and Trademark OfficeTo The Honorable Commission  
thereof.

100831000

Record the attached original documents or copy

## 1. Name of conveying party(ies):

Alessandra Eleuteri, Daniel C. Capaldi and Vasulinga  
T. Ravikumar

## 2. Name and address of receiving party(ies):

Name: ISIS Pharmaceuticals, Inc.

Street Address: 2292 Faraday Avenue

City: Carlsbad

State: California

ZIP: 92008

Additional name(s) &amp; address attached? ( ) YES (X) NO

Additional name(s) of conveying party(ies)  
attached? ( ) YES (X) NO

## 3. Nature of Conveyance:

- (X) Assignment ( ) Merger  
 ( ) Security Agreement  
 ( ) Change of Name  
 ( ) Other:

Execution Date: August 3, 1998 and September 1,  
1998

## 4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s)

09/095,811 filed 6/11/98

B. Patent No.(s)

Additional numbers attached? ( ) YES (X) NO

5. Name and address of party to whom correspondence  
concerning documents should be mailed:

Name: Michael P. Straher, Esq.  
 Internal Address: WOODCOCK WASHBURN KURTZ  
 MACKIEWICZ & NORRIS LLP  
 One Liberty Place - 46th Floor  
 Philadelphia, Pennsylvania 19103-7301

Street Address: WOODCOCK WASHBURN KURTZ  
 MACKIEWICZ & NORRIS LLP  
 One Liberty Place - 46th Floor  
 1650 Market Street  
 Philadelphia, Pennsylvania 19103-7301

## 6. Total number of applications and patents involved:

One (1)

## 7. Total fee (37 CFR 3.41):.....\$40.00

- (X) Enclosed  
 ( ) Authorized to be charged to Deposit Account  
 Number 23-3050

8. Please charge any deficiency or credit any  
overpayment to Deposit Account Number 23-3050

## DO NOT USE THIS SPACE

## 9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true  
 copy of the original document.

Michael P. Straher/38,325

Name of Person Signing/Reg. No.



Signature

September 10, 1998

Date

Total number of pages including cover sheet, attachments, and document: 5

Mail documents to be recorded with required cover sheet information to:

09/17/1998 DNGUYEN 00000132 09095811

09 FC:581

40.00 DP

Commissioner of Patents and Trademarks  
 Box Assignments  
 Washington, D.C. 20231

PATENT  
Joint Inventors

DOCKET NO.: ISIS- 2852

(Pending Application;  
Serial No. Known)

A S S I G N M E N T

WHEREAS, we Alessandra Eleuteri, Daniel C. Capaldi and Vasulinga T. Ravikumar hereinafter referred to as the assignors, residing respectively at 1269 Eolus Avenue, Encinitas, California 92024, 3855 Nobel Drive, Apt. #2125, San Diego, California 92122 and 6606 Vireo Court, Carlsbad, California 92009 are the joint inventors of certain inventions or improvements for which we have made application for Letters Patent to the United States, identified as Serial No. 09/095,811, filed June 11, 1998, entitled **METHOD OF PREPARING PHOSPHORAMIDITES**; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad California 92008, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed

PATENT  
Joint Inventors

and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

 (L.S.)  
ALESSANDRA ELEUTERI

 (L.S.)  
DANIEL C. CAPALDI

 9/1/98 (L.S.)  
VASULINGA T. RAVIKUMAR



PATENT  
Joint Inventors

[WHERE ALL INVENTORS SIGN BEFORE THE SAME NOTARY:]

\_\_\_\_\_: SS  
COUNTY OF \_\_\_\_\_:

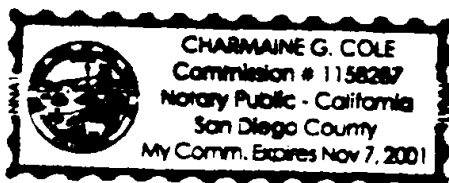
On this \_\_\_\_\_ day of \_\_\_\_\_, 19\_\_\_\_, before me personally came the above named Alessandra Eleuteri, Daniel C. Capaldi and Vasulinga T. Ravikumar to me personally known and known to me to be the same individual who executed the foregoing assignment, and who acknowledged to me that execution of the same was of that person's own free will for the use and purposes therein set forth.

\_\_\_\_\_  
Notary Public

[WHERE INVENTORS SIGN BEFORE SEPARATE NOTARIES:]

State of California:  
COUNTY OF San Diego: SS

On this 3rd day of August, 1998, before me personally came the above named Alessandra Eleuteri to me personally known and known to me to be the same individual who executed the foregoing assignment, and who acknowledged to me that execution of the same was of that person's own free will for the use and purposes therein set forth.



Charmaine G. Cole  
\_\_\_\_\_  
Notary Public

PATENT  
Joint Inventors

State of California

COUNTY OF San Diego : SS

On this 3rd day of August, 1998, before me personally came the above named Daniel C. Capaldi to me personally known and known to me to be the same individual who executed the foregoing assignment, and who acknowledged to me that execution of the same was of that person's own free will for the use and purposes therein set forth.

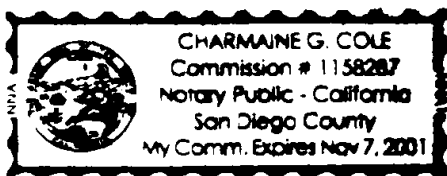


Charmaine G. Cole  
Notary Public

State of California

COUNTY OF San Diego : SS

On this 1st day of September, 1998 before me personally came the above named Vasulinga T. Ravikumar to me personally known and known to me to be the same individual who executed the foregoing assignment, and who acknowledged to me that execution of the same was of that person's own free will for the use and purposes therein set forth.



Charmaine G. Cole  
Notary Public